EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	383	548/486.ccls.	USPAT	OR	ON	2007/01/12 11:35
L2	72	l1 and indol and pyrrolidin$	USPAT	OR	ON	2007/01/12 11:36
L3	62	l2 and (crystal$ or polymorph$)	USPAT	OR	ON	2007/01/12 11:39
S1	0	WO-2001045689-$.did.	USPAT; DERWENT	OR	ON	2007/01/12 08:20
S2	1	WO-200145689-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 09:04
S3	0	WO-2001060814-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 09:05
S4	1	WO-200160814-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 09:17
S5	0	WO-2002081466-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 09:17
S6	1	WO-200281466-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 09:20
S7	1022	(method and treating and leukemia).clm.	USPAT	OR	ON	2006/09/19 09:20
S8	586	S7 and @py<"2002"	USPAT	OR	ON	2006/09/19 09:31
S9	1	WO-2003015608-$.did.	USPAT; DERWENT	OR	ON	2006/09/19 10:39
S10	0	WO-2001045689-$.did.	USPAT; DERWENT	OR	ON	2007/01/11 15:11
S11	1	WO-200145689-$.did.	USPAT; DERWENT	OR	ON	2007/01/11 15:11
S12	2	"6573293".pn.	USPAT; DERWENT	OR	ON	2007/01/11 15:16
S13	2	"20020010203".pn.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/01/12 08:20
S14	19	("20020010203"|"20030100555"|"20030130280"|"20040063773"|"6333333"|"6451838"|"6482848"|"6573293"|"6710067").PN.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/01/12 08:21
S15	9	("20020010203"|"20030100555"|"20030130280"|"20040063773"|"6333333"|"6451838"|"6482848"|"6573293"|"6710067").PN.	US-PGPUB; USPAT	OR	ON	2007/01/12 08:25

Application No: 10/776,337

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptabf1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS	9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS	10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	15	DEC 18	CA/CAplus patent kind codes updated
NEWS	16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS	17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS	19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:29:10 ON 12 JAN 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:29:23 ON 12 JAN 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 11 JAN 2007 HIGHEST RN 917345-85-8
DICTIONARY FILE UPDATES: 11 JAN 2007 HIGHEST RN 917345-85-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

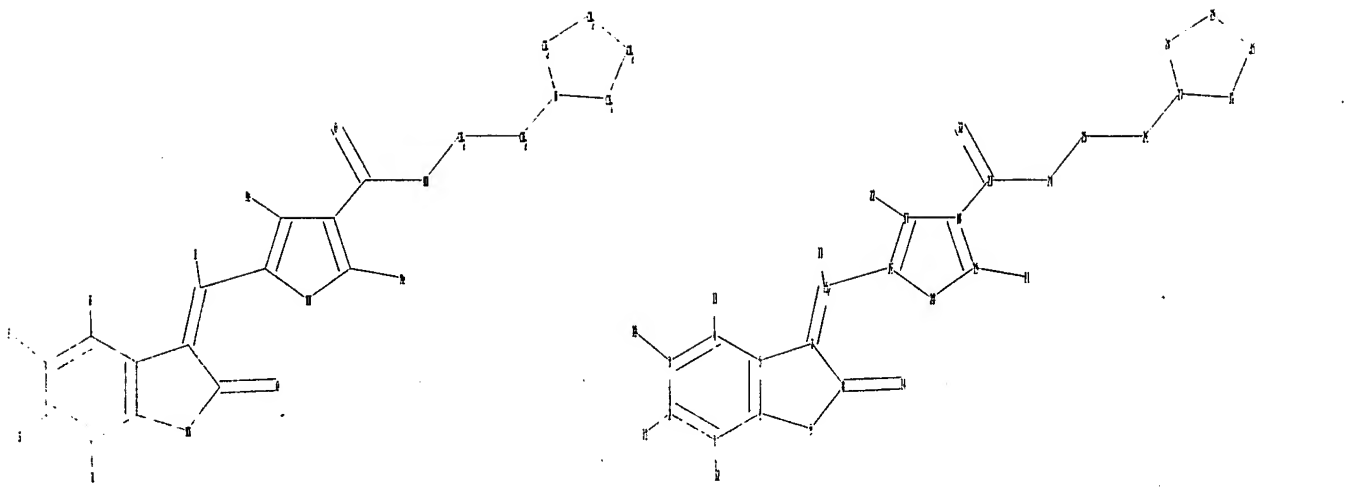
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10776337\b.str



chain nodes :
10 11 12 13 14 15 21 22 23 24 25 26 32 33
ring nodes :
1 2 3 4 5 6 7 8 9 16 17 18 19 20 27 28 29 30 31
chain bonds :
1-12 2-11 3-10 4-13 7-15 8-14 15-16 15-33 17-22 18-23 19-21 23-24 23-32 24-25 25-26 26-27
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 16-17 16-20 17-18 18-19 19-20 27-28 27-31 28-29 29-30 30-31
exact/norm bonds :
5-7 6-9 7-8 8-9 8-14 16-17 16-20 17-18 18-19 19-20 23-24 23-32 27-28 27-31 28-29 29-30 30-31
exact bonds :
1-12 2-11 3-10 4-13 7-15 15-16 15-33 17-22 18-23 19-21 24-25 25-26 26-27
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:CLASS 33:CLASS

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:29:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3 TO ITERATE

100.0% PROCESSED 3 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3 TO 163
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 11:29:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 62 TO ITERATE

100.0% PROCESSED 62 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'HCAPLUS' ENTERED AT 11:29:55 ON 12 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 12 Jan 2007 VOL 146 ISS 4
FILE LAST UPDATED: 11 Jan 2007 (20070111/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l3
L4          22 L3

=> s l4 and (crystal or polymorph)
UNMATCHED RIGHT PARENTHESIS ')'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l4 and (crystal? or polymorph?)
       1820813 CRYSTAL?
        350998 CRYST
          1801 CRYSTS
        352266 CRYST
                 (CRYST OR CRYSTS)
         90586 CRYSTD
         19455 CRYSTG
        236830 CRYSTN
          2400 CRYSTNS
        238144 CRYSTN
                 (CRYSTN OR CRYSTNS)
       2124079 CRYSTAL?
                 (CRYSTAL? OR CRYST OR CRYSTD OR CRYSTG OR CRYSTN)
        200093 POLYMORPH?
L5           1 L4 AND (CRYSTAL? OR POLYMORPH?)

=> d ibib

L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:740292  HCAPLUS
DOCUMENT NUMBER:          141:265970
TITLE:                    Polymorphs of pyrrole-substituted
                          2-indolinone protein kinase inhibitors
INVENTOR(S):              Sun, Changquan; Foster, Todd P.; Han, Fusen; Hawley,
                          Michael; Thamann, Tom
PATENT ASSIGNEE(S):       Pharmacia & Upjohn Company, USA
SOURCE:                   PCT Int. Appl., 36 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004076410         A2    20040910    WO 2004-US5281          20040223
     WO 2004076410         A3    20050303
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004259929         A1    20041223    US 2004-776337          20040212
     NL 1025551            A1    20040826    NL 2004-1025551         20040223
     NL 1025551            C2    20050314
     AU 2004215407         A1    20040910    AU 2004-215407          20040223
     CA 2516900            A1    20040910    CA 2004-2516900         20040223
     EP 1599200            A2    20051130    EP 2004-713716          20040223
```

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         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2004007795          A     20060214    BR 2004-7795              20040223
     CN 1771032             A     20060510    CN 2004-80005021          20040223
     JP 2006518755          T     20060817    JP 2006-503796            20040223
     NO 2005004071          A     20051013    NO 2005-4071              20050901
PRIORITY APPLN. INFO.:                         US 2003-448863P      P   20030224
                                               US 2004-776337       A   20040212
                                               WO 2004-US5281       A   20040223


=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     6.38     178.69

STN INTERNATIONAL LOGOFF AT 11:30:59 ON 12 JAN 2007
```

Application No: 10/776,337

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptabf1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 4	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 5	MAY 11	KOREAPAT updates resume
NEWS 6	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS 7	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 8	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS 9	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS 10	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS 11	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12	JUl 11	CHEMSAFE reloaded and enhanced
NEWS 13	JUl 14	FSTA enhanced with Japanese patents
NEWS 14	JUl 19	Coverage of Research Disclosure reinstated in DWPI
NEWS 15	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 16	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 17	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18	SEP 11	CA/CAplus enhanced with more pre-1907 records

NEWS EXPRESS	JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:00:09 ON 19 SEP 2006

Application No: 10/776,337

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:00:24 ON 19 SEP 2006
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STRUCTURE FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1
DICTIONARY FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

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Effective September 24, 2006, Concord 3D coordinates will no longer be available. Please contact CAS Customer Care (http://www.cas.org/supp.html) if you have a need for 3D coordinates.

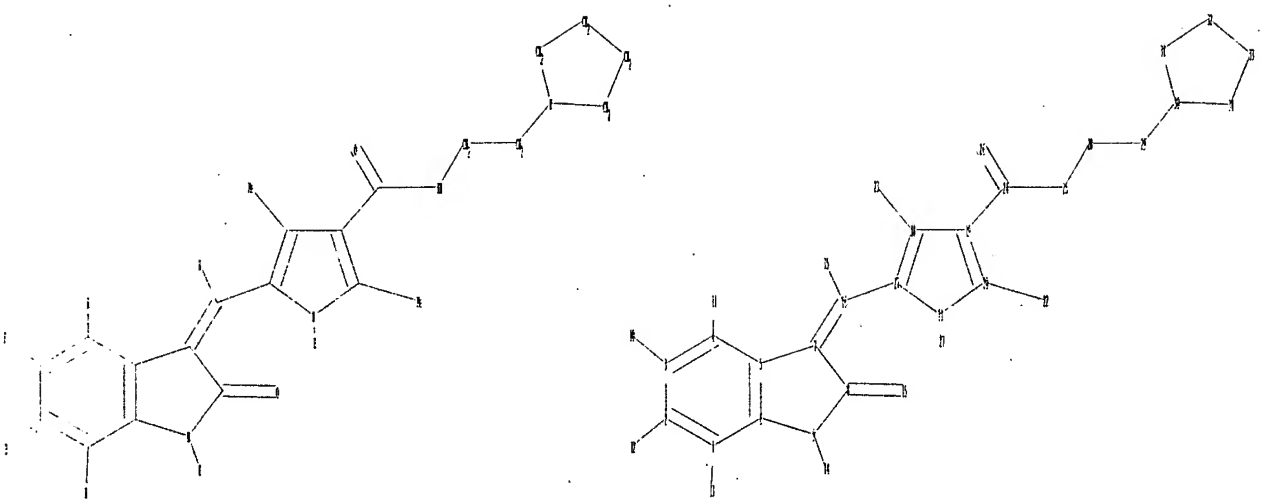
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10776337\a.str



chain nodes :
10 11 12 13 14 15 16 22 23 24 25 26 27 28 29 35
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 30 31 32 33 34
chain bonds :
1-13 2-12 3-10 4-11 7-16 8-15 9-14 16-17 16-35 18-23 19-24 20-22 21-27
24-25 24-26 25-28 28-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
30-31 30-34 31-32 32-33 33-34
exact/norm bonds :
5-7 6-9 7-8 8-9 8-15 17-18 17-21 18-19 19-20 20-21 24-25 24-26 30-31
30-34 31-32 32-33 33-34
exact bonds :
1-13 2-12 3-10 4-11 7-16 9-14 16-17 16-35 18-23 19-24 20-22 21-27 25-28
28-29 29-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom
19:Atom 20:Atom 21:Atom 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:CLASS

L1 STRUCTURE UPLOADED

```
=> d
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 09:00:50 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED         3 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 09:00:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       62 TO ITERATE

100.0% PROCESSED        62 ITERATIONS                                 5 ANSWERS
SEARCH TIME: 00.00.01

L3            5 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   166.94     167.15

FILE 'HCAPLUS' ENTERED AT 09:00:58 ON 19 SEP 2006
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FILE COVERS 1907 - 19 Sep 2006  VOL 145 ISS 13
FILE LAST UPDATED: 18 Sep 2006  (20060918/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
```

substance identification.

=> s l3
L4 16 L3

=> d ibib abs hitstr 1-16

L4 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:33320 HCAPLUS
DOCUMENT NUMBER: 144:108206
TITLE: Method of synthesizing indolinone compounds
INVENTOR(S): Havens, Jeffrey L.; Vaidyanathan, Rajappa
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006009510	A1	20060112	US 2005-174892		20050705
PRIORITY APPLN. INFO.:			US 2004-586865P	P	20040709

OTHER SOURCE(S): MARPAT 144:108206
GI

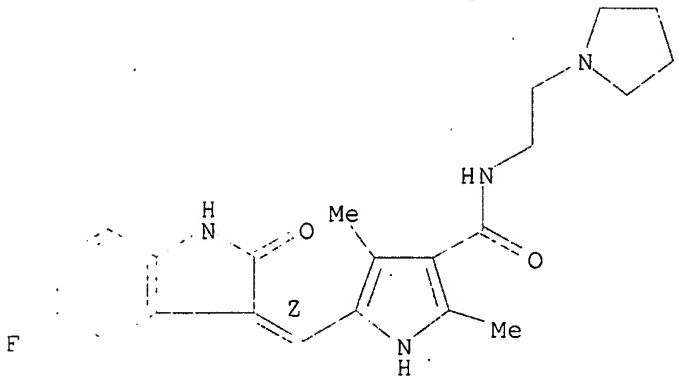
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for the preparation of indolinone compds. of formula I [R1 = -(CH2)mR9 and one or more hydrogens in the -(CH2)m groups is optionally substituted by -OH; R2 = H or C1-12alkyl; optionally, R1 and R2, together with the nitrogen to which they are attached, can join to form a 5, 6, or 7-membered heterocyclic group optionally containing an addnl. N, O, or S ring atom; R3 and R4 = independently C1-12alkyl; R5, R6, R7, and R8 = independently H, C1-12alkyl, C1-12alkoxy, C3-12cycloalkyl, etc.; R9 = (un)substituted amine, -OH, C6-12aryl, C6-12alkaryl, etc.; m = 0-4], via a synthetic route wherein the amide sidechain on the pyrrole moiety is attached prior to pyrrole formation, is reported. Thus, diketene was ring-opened with N,N-diethylethylenediamine to form N-[2-(diethylamino)ethyl]-3-oxobutanamide which was treated with the oxime of t-Bu acetoacetate to give the pyrrole II in 53% yield. Pyrrole II is then decarboxylated and reacted with an oxindole and a formylating agent to provide III in 74% yield. The compds. of formula I are useful in the treatment of abnormal cell growth, such as cancer (no data).

IT 356068-94-5P 874819-74-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of indolinone compds. useful in treatment of abnormal cell growth)

RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

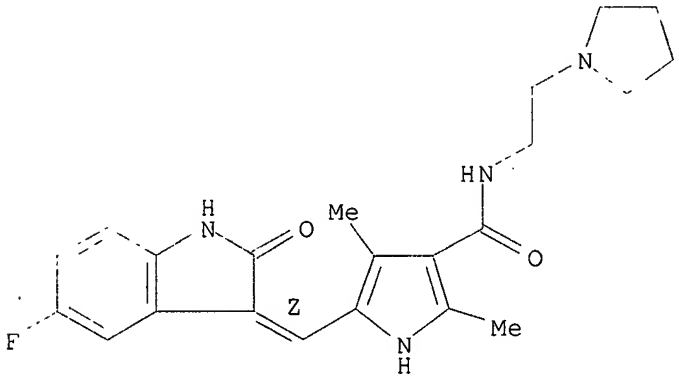


RN 874819-74-6 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

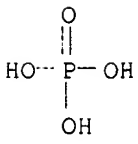
CRN 356068-94-5
CMF C22 H25 F N4 O2

Double bond geometry as shown.



CM 2

CRN 7664-38-2
CMF H3 O4 P



L4 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:878170 HCAPLUS
DOCUMENT NUMBER: 141:366237
TITLE: Preparation of indolinone compounds for treatment of excessive osteolysis
INVENTOR(S): Murray, Lesley; O'Farrell, Anne-Marie; Abrams, Tinya
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004209937	A1	20041021	US 2004-780917	20040219
AU 2004216188	A1	20040910	AU 2004-216188	20040223
CA 2516786	AA	20040910	CA 2004-2516786	20040223
WO 2004075775	A2	20040910	WO 2004-US405283	20040223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004075775	A2	20040910	WO 2004-US5283	20040223
WO 2004075775	A3	20050414		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1599207	A2	20051130	EP 2004-713729	20040223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007793	A	20060214	BR 2004-7793	20040223
CN 1758914	A	20060412	CN 2004-80006758	20040223
JP 2006518756	T2	20060817	JP 2006-503797	20040223

PRIORITY APPLN. INFO.:

US 2003-448861P	P	20030224
US 2004-780917	A	20040219
WO 2004-US5283	A	20040223

OTHER SOURCE(S): MARPAT 141:366237
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is a method for treating excessive osteolysis in a patient, comprising administering to said patient an effective amount of a compound of formula (I) [wherein R = H, OH, alkyl, aryl, cycloalkyl, heteroaryl, alkoxy, heterocyclyl, amino; R1 = alkyl, halo, aryl, alkoxy, haloalkyl,

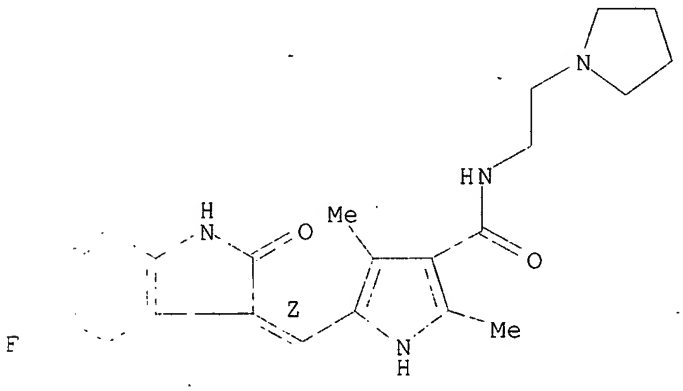
haloalkoxy, cycloalkyl, heteroaryl, heterocyclyl, HO, COR8, NR9R10, NR9COR12, CONR9R10; R2 = alkyl, aryl, heteroaryl, COR8, SO2R''; (wherein R" = alkyl, aryl, heteroaryl, NR9R10, alkoxy); R5 = H, alkyl, aryl, haloalkyl, cycloalkyl, heteroaryl, heterocyclyl, HO, COR8, (CHR)rR11; X = O, S; p, r = 0-3; q = 0-2; wherein R8 = OH, alkyl, aryl, heteroaryl, alkoxy, cycloalkyl, heterocyclyl; R9, R10 = H, alkyl, aryl, aminoalkyl, heteroaryl, cycloalkyl, heterocyclyl; or NR9R10 together forms a ring consisting of the ring atoms selected from the group consisting of C, N, O, and S; R11 = OH, NH2, mono- or disubstituted amino, alkyl, aryl, heteroaryl, alkoxy, cycloalkyl, heterocyclyl; R12 = alkyl, aryl, heteroaryl, alkoxy, cycloalkyl, heterocyclyl; Z = OH, O-alkyl, NR3R4; wherein R3, R4 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl; or NR3R4 forms a ring consisting of the ring atoms selected from the group consisting of CH2, N, O, and S, or Q1; wherein Y = CH2, O, N, S; Q = C, N; n = 0-4; m = 0-3] or salts thereof. These compds. are useful for treating excessive osteolysis, by inhibiting M-CSF mediated osteoclast development. They are useful for inhibiting phosphorylation of colony-stimulating factor-1 receptor (CSF1R), and for treating cancers that express CSF1R. Thus, in a study on bone metastasis of cancer, 5-(5-Fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide (II) at 80 or 40 mg/kg per day for 21 days inhibited the growth of 435/HAL-luc breast cancer cells in bone by 89% in mice in 41 days after inoculation with cancer cells. Formulations, e.g. hard gelatin capsule containing II, were described.

IT 356068-94-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolinone compds. for treatment of excessive osteolysis, inhibiting phosphorylation of colony-stimulating factor-1 receptor (CSF1R), and treating cancers that express CSF1R)

RN 356068-94-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L4 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:740292 HCAPLUS
DOCUMENT NUMBER: 141:265970
TITLE: Polymorphs of pyrrole-substituted 2-indolinone protein kinase inhibitors

INVENTOR(S): Sun, Changquan; Foster, Todd P.; Han, Fusen; Hawley, Michael; Thamann, Tom
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004076410	A2	20040910	WO 2004-US5281	20040223
WO 2004076410	A3	20050303		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004259929	A1	20041223	US 2004-776337	20040212
NL 1025551	A1	20040826	NL 2004-1025551	20040223
NL 1025551	C2	20050314		
AU 2004215407	A1	20040910	AU 2004-215407	20040223
CA 2516900	AA	20040910	CA 2004-2516900	20040223
EP 1599200	A2	20051130	EP 2004-713716	20040223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007795	A	20060214	BR 2004-7795	20040223
CN 1771032	A	20060510	CN 2004-80005021	20040223
JP 2006518755	T2	20060817	JP 2006-503796	20040223
NO 2005004071	A	20051013	NO 2005-4071	20050901

PRIORITY APPLN. INFO.:		
US 2003-448863P	P	20030224
US 2004-776337	A	20040212
WO 2004-US5281	A	20040223

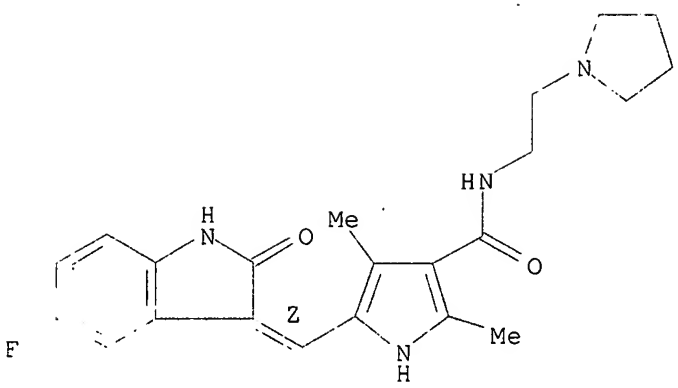
AB The present invention relates to polymorphs of the 3-pyrrole-substituted 2-indolinone, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-pyrrolidin-1-ylethyl)amide (I). The phys. properties of polymorphs of I were determined by spectroscopic methods.

IT 753451-03-5
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(polymorphs of pyrrole-substituted indolinone protein kinase inhibitors)

RN 753451-03-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

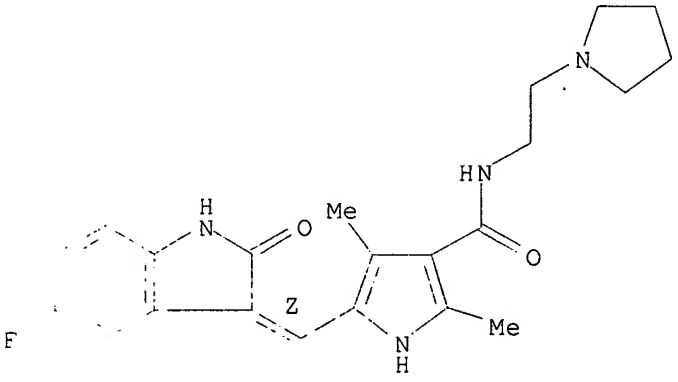
Double bond geometry as shown.



● HCl

IT 356068-94-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphs of pyrrole-substituted indolinone protein kinase inhibitors)
RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

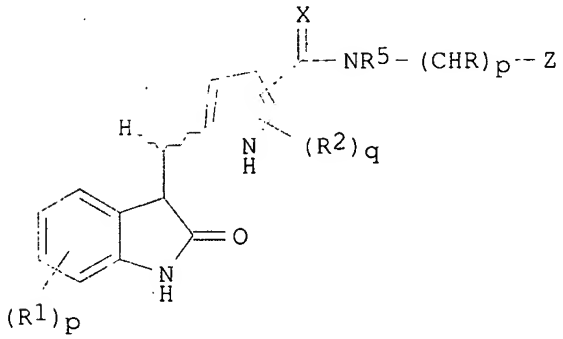


L4 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:452964 HCAPLUS
DOCUMENT NUMBER: 141:1206
TITLE: Combination administration of an indolinone with a chemotherapeutic agent for cell proliferation disorders
INVENTOR(S): Abrams, Tinya; Murray, Lesley; Pryer, Nancy; Cherrington, Julie M.
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045523	A2	20040603	WO 2003-US36526	20031114
WO 2004045523	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1024779	A1	20040518	NL 2003-1024779	20031114
NL 1024779	C2	20041109		
CA 2506308	AA	20040603	CA 2003-2506308	20031114
AU 2003290943	A1	20040615	AU 2003-290943	20031114
US 2004152759	A1	20040805	US 2003-712296	20031114
EP 1562600	A2	20050817	EP 2003-783527	20031114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015630	A	20050823	BR 2003-15630	20031114
CN 1711089	A	20051221	CN 2003-80103225	20031114
JP 2006508981	T2	20060316	JP 2004-553729	20031114
NO 2005002578	A	20050527	NO 2005-2578	20050527
PRIORITY APPLN. INFO.:			US 2002-426386P P	20021115
			WO 2003-US36526 W	20031114

OTHER SOURCE(S): MARPAT 141:1206
GI



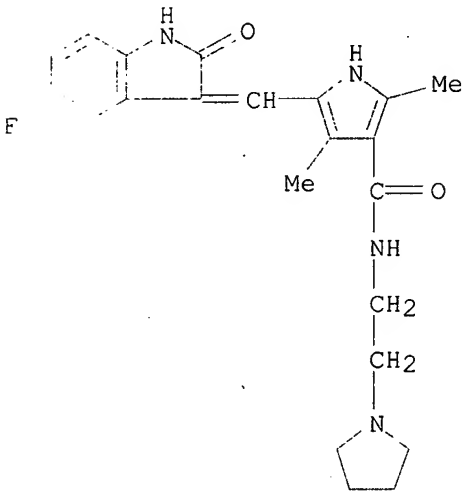
I

AB The invention relates to a method of treating cancer by administering a combination of an indolinone compound with another chemotherapeutic agent. The combination of an indolinone compound I (R = H, OH, alkyl, aryl, cycloalkyl, heteroaryl, alkoxy, heterocycle, amino; R1 = alkyl, halo, alkoxy, etc.; R2 = alkyl, aryl, heteroaryl, etc.; R5 = H, alkyl, aryl, haloalkyl, cycloalkyl, etc.; X = O, S; p = 0, 1, 2, 3; q = 0, 1, 2; Z = OH, -O-alkyl, -NR3R4; R3, R4 = H, alkyl, aryl, heteroaryl, cycloalkyl,

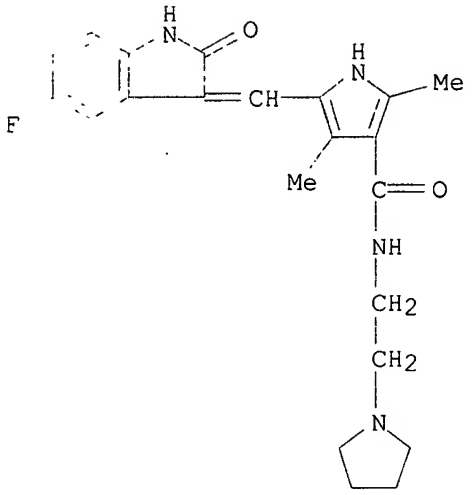
heterocycle, or together with N form a ring) with another chemotherapeutic agent provides an enhanced effect in treating cancer patients. Mice implanted with MX-1 human breast carcinoma fragments were treated with docetaxel and 5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide (preparation given).

IT 346405-32-1 346405-32-1D, acceptable salts, solvates, hydrates
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as indolinone compound; cancer therapy using combination administration of indolinone compds. with chemotherapeutic agents for cell proliferation disorders)

RN 346405-32-1 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 346405-32-1 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



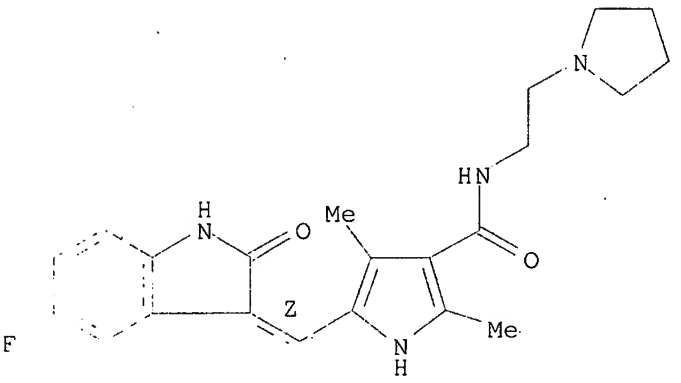
L4 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:943094 HCAPLUS
DOCUMENT NUMBER: 141:33400
TITLE: Proof of target for SU11654: inhibition of KIT phosphorylation in canine mast cell tumors
AUTHOR(S): Pryer, Nancy K.; Lee, Leslie B.; Zadovaskaya, Regina; Yu, Xiaoming; Sukbuntherng, Juthamas; Cherrington, Julie M.; London, Cheryl A.
CORPORATE SOURCE: SUGEN,Inc, South San Francisco, CA, USA
SOURCE: Clinical Cancer Research (2003), 9(15), 5729-5734
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to evaluate the effect of the receptor tyrosine kinase inhibitor SU11654 on the activity of its mol. target KIT in canine mast cell tumors (MCT) and correlate target inhibition with mutational status of the c-kit juxtamembrane domain and SU11654 plasma concentration Tumor biopsies were obtained from dogs with advanced MCTs before and 8 h after administration of a single oral dose of SU11654, previously shown to be active in dogs with MCTs. Blood samples were taken to determine the plasma concentration of SU11654. Levels of phosphorylated KIT and ERK1/2 were assessed in tumor biopsies by Western blot. Tumors were analyzed by PCR for the presence or absence of an internal tandem duplication (ITD) in the juxtamembrane domain of c-kit. Fourteen dogs with advanced MCTs were enrolled in the study; 11 of these were evaluable for KIT target modulation (the remaining tumor specimens had inevaluable amts. of total KIT protein). Of these, eight MCTs showed reduced levels of phosphorylated KIT relative to total KIT after treatment with SU11654, compared with pretreatment biopsies. All four evaluable MCTs expressing ITD mutant c-kit showed modulation of KIT phosphorylation, as did four of seven tumors expressing non-ITD c-kit. Phosphorylated ERK1/2 was modulated in seven tumors; this did not correlate with inhibition of KIT phosphorylation. SU11654 treatment at the efficacious dose results in inhibition of KIT phosphorylation in canine MCTs.

IT 356068-94-5, SU11654
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(SU11654 effect on activity of mol. target KIT in canine mast cell tumors)
RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:931518 HCAPLUS
DOCUMENT NUMBER: 140:689
TITLE: Genes showing altered patterns of expression in response to inhibition of tyrosine kinases and their use in screening kinase inhibitors
INVENTOR(S): Morimoto, Alyssa; Deprimo, Samuel; O'Farrell, Anne-Marie; Smolich, Beverly D.; Manning, William C.; Walter, Sarah A.; Schilling, James Walter, Jr.; Cherrington, Julie
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097854	A2	20031127	WO 2003-US15711	20030519

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003233576	A1	20031202	AU 2003-233576		20030519
US 2004018528	A1	20040129	US 2003-440464		20030519
PRIORITY APPLN. INFO.:			US 2002-380872P	P	20020517
			US 2003-448874P	P	20030224
			US 2003-448922P	P	20030224
			WO 2003-US15711	W	20030519

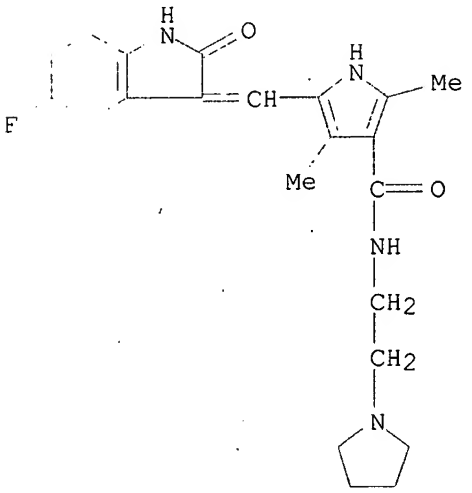
OTHER SOURCE(S): MARPAT 140:689

AB Genes that are regulated by tyrosine kinase-dependent signal transduction pathways are identified as markers for the screening of inhibitors of kinase activity. The change in levels of either the protein or mRNA in a suitable test system may be used to assess the effectiveness of a test compound as an inhibitor of a tyrosine kinase activity. The invention also relates to novel methods, wherein a change in the level of at least one biomarker in a mammal exposed to a compound, compared to the level of the biomarker(s) in a mammal that has not been exposed to the compound, indicates whether the mammal is being exposed to, or is experiencing or will experience a therapeutic or toxic effect in response to, a compound that inhibit tyrosine kinase activity.

IT 346405-32-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as tyrosine kinase inhibitor; genes showing altered patterns of expression in response to inhibition of tyrosine kinases and their use in screening kinase inhibitors)

RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:678808 HCAPLUS
DOCUMENT NUMBER:	139:214331
TITLE:	Process for preparing aminocarbonylpyrrolylmethylidene indolinones from indolinones, imidazolcarbonylpyrrolecarboxaldehydes, and amines.
INVENTOR(S):	Jin, Qingwu; Mauragis, Michael A.; May, Paul D.
PATENT ASSIGNEE(S):	Pharmacia & Upjohn Company, USA
SOURCE:	PCT Int. Appl., 51 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070725	A2	20030828	WO 2003-US4520	20030214
WO 2003070725	A3	20040115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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WO 2002066463	A1	20020829	WO 2002-US4407	20020215
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475455	AA	20030828	CA 2003-2475455	20030214
AU 2003216282	A1	20030909	AU 2003-216282	20030214
EP 1476443	A2	20041117	EP 2003-742760	20030214
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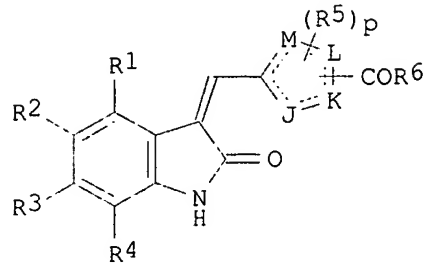
BR 2003007721	A	20050125	BR 2003-7721	20030214
CN 1671693	A	20050921	CN 2003-803988	20030214
JP 2005528344	T2	20050922	JP 2003-569632	20030214
PRIORITY APPLN. INFO.:			WO 2002-US4407 A	20020215
			US 2002-411732P P	20020918
			US 2001-268683P P	20010215
			US 2001-312361P P	20010815
			WO 2003-US4520 W	20030214

OTHER SOURCE(S): CASREACT 139:214331; MARPAT 139:214331
GI



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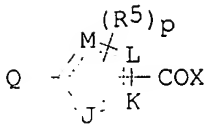

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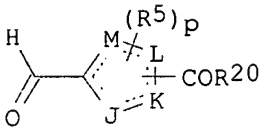


III

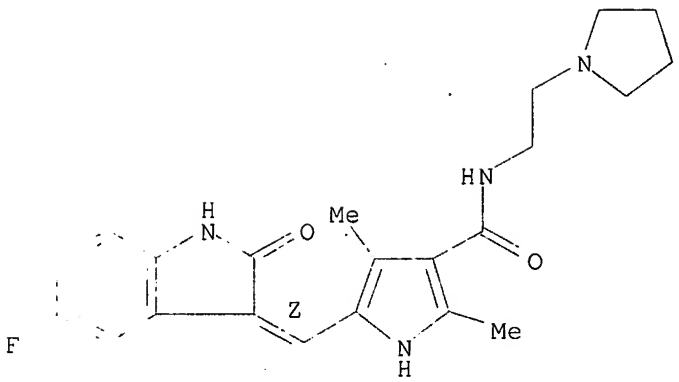
AB Title compds. [I; R1-R5 = H, alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl containing 1-3 N, S, O, aryloxy, alkaryl, alkaryloxy, halo, trihalomethyl, OH, SOR', SO2NR'R'', SO3R', SR', NO2, NR'R'', CN, COR', O2CR', NHCOR', (CH2)nCO2R', CONR'R"; R6 = NR8(CH2)mR9, NR10R11, 1-2 of the CH2 groups may be substituted by OH, halo; R8 = H, alkyl; R9 = NR10R11, OH, COR12, aryl, heterocyclyl containing 1-3 N, S, O, N+(O-)R10, NHCOR13; R10, R11 = H, alkyl, cyanoalkyl, cycloalkyl, aryl, heterocyclyl containing 1-3 N, S, O; R10R11N = (R'-substituted) 5-6 membered heterocyclyl optionally containing 1-3 addnl. N, O, S; R12 = H, OH, alkoxy, aryloxy; R13 = alkyl, haloalkyl, aralkyl; R', R" = H, alkyl, cyanoalkyl, cycloalkyl, aryl, heterocyclyl containing 1-3 N, S , O; R'R"N = 5-6 membered heterocyclyl optionally containing 1-3 addnl. N, O, S; halo = F, Cl, Br, iodo; J = O, S, NH; 1 of K, L, M = CCOR6, the others of K, L, M = CR5, CR52, N, NR5, O, S; n, p = 0-2; m = 1-4], were prepared The process comprises reaction of azoles (II) with X2R (R5, J, K, L, M, p are as defined above; Q = CHO, CHS, dioxolanyl, tetrahydrooxazolyl, etc.; X1 = Cl, Br; X2 = H; R = pyrrolyl, thiazolidinethionyl, oxazolidinethionyl, imidazolidinethionyl, pyrrolidinethionyl, etc.; or X1 = OH, alkoxy, PhO; X2 = imidazolecarbonyl; R = imidazolyl) to give (III; R20 = OR, R), and reaction of III with HR6 (R6 as defined above) and the corresponding indolinone. Thus, 4-(1H-imidazol-1-ylcarbonyl)-3,5-dimethyl-1H-pyrrole-2-carboxaldehyde, N,N-diethylethylenediamine, 5-fluorooxindole, Et3N, and MeCN were mixed and heated for 18 h at 60° to give 85% N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide.

IT 356068-94-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing aminocarbonylpyrrolylmethylideneindolinones from indolinones, imidazolcarbonylpyrrolecarboxaldehydes, and amines)

RN 356068-94-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

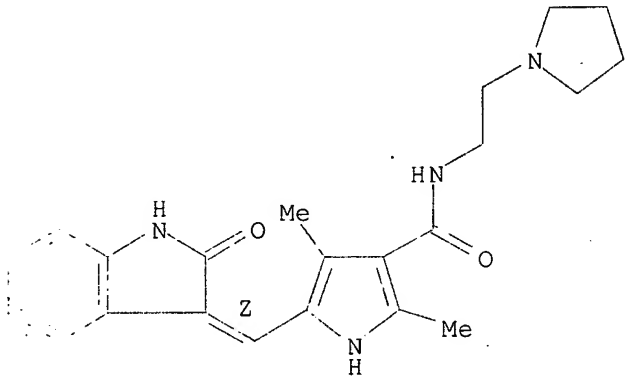


L4 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:528824 HCAPLUS
DOCUMENT NUMBER: 140:70428
TITLE: Phase I dose-escalating study of SU11654, a small molecule receptor tyrosine kinase inhibitor, in dogs with spontaneous malignancies
AUTHOR(S): London, Cheryl A.; Hannah, Alison L.; Zadovoskaya, Regina; Chien, May B.; Kollias-Baker, Cynthia; Rosenberg, Mona; Downing, Sue; Post, Gerald; Boucher, Joseph; Shenoy, Narmada; Mendel, Dirk B.; McMahon, Gerald; Cherrington, Julie M.
CORPORATE SOURCE: School of Veterinary Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Clinical Cancer Research (2003), 9(7), 2755-2768
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of the following study was to investigate the safety and efficacy of the novel multitargeted indolinone receptor tyrosine kinase (RTK) inhibitor, SU11654, using a canine model of spontaneous tumors. This p.o. bioavailable compound exhibits potent inhibitory activity against members of the split kinase family of RTKs, including vascular endothelial growth factor receptor, platelet-derived growth factor receptor, Kit, and Flt-3, resulting in both direct antitumor and antiangiogenic activity. This was a Phase I trial in which successive cohorts of dogs with spontaneous tumors that had failed standard treatment regimens received escalating doses of SU11654 as oral therapy. Pharmacokinetics, toxicity, and tumor response were assessed. Fifty-seven dogs with a variety of cancers were enrolled; of these, 10 experienced progressive disease within the first 3 wk. Measurable objective responses were observed in 16 dogs (including 6 complete responses), primarily in mast cell tumors (n = 11), mixed mammary carcinomas (n = 2), soft tissue sarcomas (n = 2), and multiple myeloma (n = 1), for an overall response rate of 28% (16 of 57). Stable disease of sufficient duration to be considered clin. meaningful (>10 wk) was seen in an addnl. 15 dogs, for a resultant overall biol. activity of 54% (31 of 57). This study provides the first evidence that p.o. administered kinase inhibitors can exhibit activity against a variety of spontaneous malignancies. Given the similarities of canine and human cancers with regard to tumor biol. and the presence of analogous RTK dysregulation, it is likely that such agents will demonstrate comparable antineoplastic activity in people.

IT 356068-94-5, SU11654
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. receptor tyrosine kinase inhibitor SU11654 in dogs with spontaneous malignancies)
RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:334853 HCAPLUS
DOCUMENT NUMBER: 138:331677
TITLE: Treatment of acute myeloid leukemia with indolinone compounds, and preparation thereof
INVENTOR(S): O'Farrell, Ann-Marie; Cherrington, Julie
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

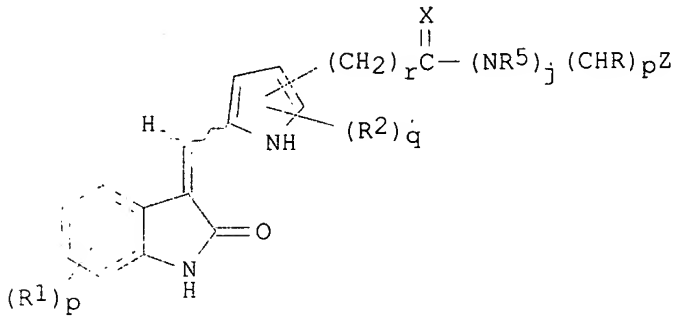
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035009	A2	20030501	WO 2002-US34525	20021028
WO 2003035009	A3	20040318		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2464790	AA	20030501	CA 2002-2464790		20021028
US 2003130280	A1	20030710	US 2002-281266		20021028
EP 1446117	A2	20040818	EP 2002-795563		20021028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002013960	A	20040831	BR 2002-13960		20021028
JP 2005511540	T2	20050428	JP 2003-537578		20021028
NZ 532405	A	20051223	NZ 2002-532405		20021028
ZA 2004003091	A	20050114	ZA 2004-3091		20040422
PRIORITY APPLN. INFO.:			US 2001-330623P	P	20011026
			WO 2002-US34525	W	20021028

OTHER SOURCE(S): MARPAT 138:331677

GI



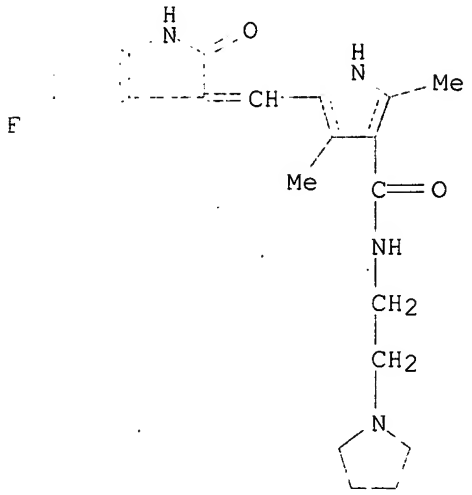
I

AB A method of treating acute myeloid leukemia in patient pos. for FLT-3-ITD is described. The treatment is accomplished by administration of an indolinone compound (Markush included). Preparation of the compds. of the invention, e.g. I, is described.

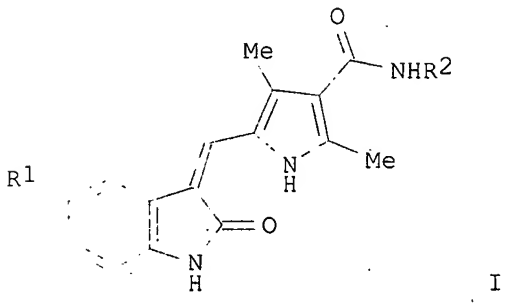
IT 346405-32-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indolinone derivative preparation for treatment of acute myeloid leukemia)

RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:170636 HCAPLUS
DOCUMENT NUMBER: 138:337929
TITLE: Discovery of 5-[5-Fluoro-2-oxo-1,2-dihydroindol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic Acid (2-Diethylaminoethyl)amide, a Novel Tyrosine Kinase Inhibitor Targeting Vascular Endothelial and Platelet-Derived Growth Factor Receptor Tyrosine Kinase
AUTHOR(S): Sun, Li; Liang, Chris; Shirazian, Sheri; Zhou, Yong; Miller, Todd; Cui, Jean; Fukuda, Juri Y.; Chu, Ji-Yu; Nematalla, Asaad; Wang, Xueyan; Chen, Hui; Sistla, Anand; Luu, Tony C.; Tang, Flora; Wei, James; Tang, Cho
CORPORATE SOURCE: SUGEN Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(7), 1116-1119
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:337929
GI



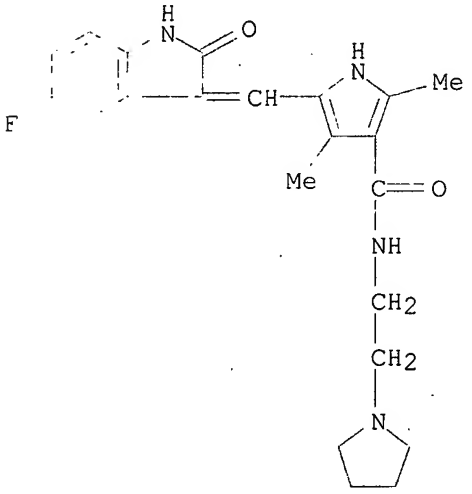
I

AB To improve the antitumor properties and optimize the pharmaceutical properties including solubility and protein binding of indolin-2-ones, a series of different basic and weakly basic pyrrolylmethylidene indolinones I [R1 = H, F, Cl, Br; R2 = Et2NCH2CH2, pyridin-4-ylmethyl, 2-(1,2,3-triazol-1-yl)ethyl, etc.] were designed and synthesized. Indolinone I [R1 = F, R2 = Et2NCH2CH2 (II)] showed the best overall profile in terms of potency for the VEGF-R2 and PDGF-Rβ tyrosine kinase at biochem. and cellular levels, solubility, protein binding, and bioavailability. II is currently in phase I clin. trials for the treatment of cancers.

IT 346405-32-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of (pyrrolylmethylidene)indolinones as tyrosine kinase inhibitors targeting vascular endothelial and platelet-derived growth factor receptor tyrosine kinase)

RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:154170 HCAPLUS
DOCUMENT NUMBER: 138:180703
TITLE: Combination therapy for the treatment of cancer
INVENTOR(S): Doshi, Parul; Cherrington, Julie
PATENT ASSIGNEE(S): Masferrer, Jaime, USA; Sugen Inc.
SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003015608	A2	20030227	WO 2002-US25797 20020815
WO 2003015608	A3	20031030	

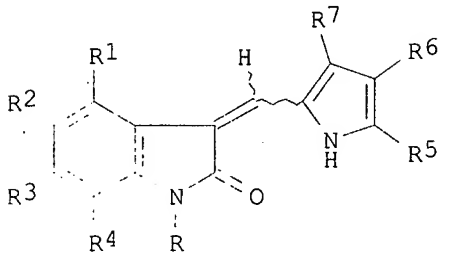
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2457745	AA	20030227	CA 2002-2457745	20020815
US 2003216410	A1	20031120	US 2002-218910	20020815
BR 2002011978	A	20040720	BR 2002-11978	20020815
CN 1541098	A	20041027	CN 2002-815912	20020815
JP 2005501843	T2	20050120	JP 2003-520373	20020815
TW 230609	B1	20050411	TW 2002-91118425	20020815
NZ 530792	A	20050930	NZ 2002-530792	20020815
ZA 2004000849	A	20050503	ZA 2004-849	20040202
NO 2004000516	A	20040413	NO 2004-516	20040204
BG 108622	A	20051031	BG 2004-108622	20040308
PRIORITY APPLN. INFO.:			US 2001-312413P P	20010815
			WO 2002-US25797 W	20020815

OTHER SOURCE(S): MARPAT 138:180703

GI



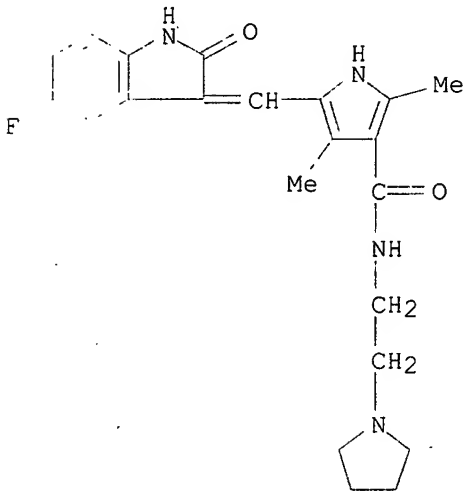
I

AB The present invention relates to methods for treatment or prevention of neoplasia disorders using protein tyrosine kinase inhibitors in combination with cyclooxygenase inhibitors, in particular cyclooxygenase-2 selective inhibitors. The protein kinase inhibitors are of the formula I where R = H, piperazin-1-ylmethyl, 4-methylpiperazin-1-ylmethyl, piperidin-1-ylmethyl, etc.; R1 = H, halo, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, etc.; R2 = hydrogen, halo, alkyl, substituted alkyl, trihalomethyl, hydroxy, alkoxy, etc.; R3 = H, halogen, alkyl, substituted alkyl, trihalomethyl, hydroxy, alkoxy, aryl, heteroaryl, etc.; R4 = H, halogen, alkyl, substituted alkyl, hydroxy, alkoxy, etc.; R5 = H, alkyl, substituted alkyl, etc.; R6 = hydrogen, alkyl, substituted alkyl, etc.; and R7 = H, alkyl, substituted alkyl, aryl, heteroaryl, etc.

IT 346405-32-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for treatment of cancer using protein tyrosine kinase inhibitors and cyclooxygenase-2 inhibitors)

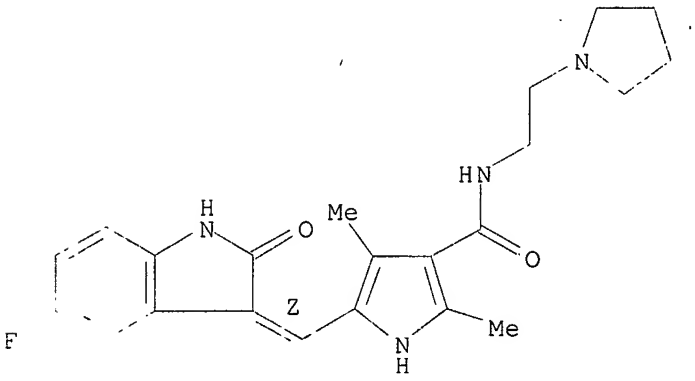
RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 356068-94-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(combination therapy for treatment of cancer using protein tyrosine kinase inhibitors and cyclooxygenase-2 inhibitors)
RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

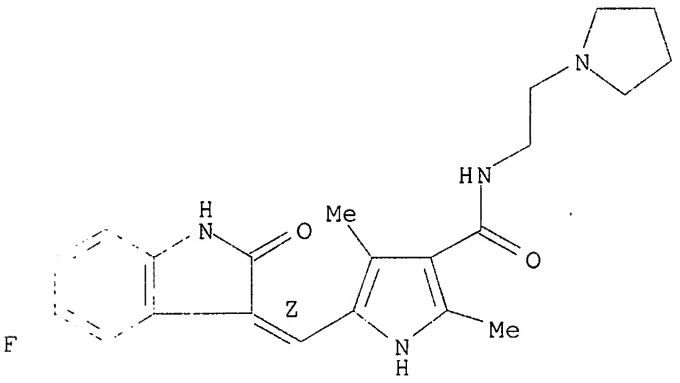
Double bond geometry as shown.



L4 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:805222 HCAPLUS
DOCUMENT NUMBER: 139:270353
TITLE: Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors. [Erratum to document cited in CA138:147266]

AUTHOR(S): Liao, Albert T.; Chien, May B.; Shenoy, Narmada; Mendel, Dirk B.; McMahon, Gerald; Cherrington, Julie M.; London, Cheryl A.
CORPORATE SOURCE: Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California at Davis, Davis, CA, 95616, USA
SOURCE: Blood (2002), 100(8), 2696
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In "Materials and methods", under "Antibodies", the fifth sentence should refer to "anti-phosphatidyl inositol 3-kinase.".
IT 356068-94-5, SU 11654
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors (Erratum))
RN 356068-94-5 HCAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



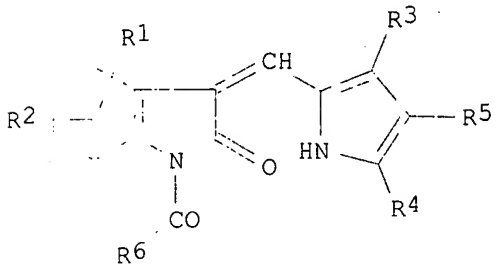
L4 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:793619 HCAPLUS
DOCUMENT NUMBER: 137:294870
TITLE: Preparation of prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinones and activity as modulators of protein kinases
INVENTOR(S): Sun, Connie Li; Wei, Chung Chen; Tang, Peng Cho; Koenig, Marcel; Zhou, Yong; Vojkovsky, Tomas; Nematalla, Asaad S.
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002081466	A1	20021017	WO 2002-US11001 20020409
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW		
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
US 2003100555	A1	20030529	US 2002-118321 20020409
US 6797725	B2	20040928	
US 2004186161	A1	20040923	US 2004-816957 20040405
US 7053114	B2	20060530	
PRIORITY APPLN. INFO.:			US 2001-282630P P 20010409
			US 2002-118321 A3 20020409

OTHER SOURCE(S): MARPAT 137:294870

GI



I

AB The present invention relates to pyrrole substituted 2-indolinone compds. (shown as I; e.g. 3-[1-(3,5-dimethyl-1H-pyrrol-2-yl)meth-(Z)-ylidene]-2-oxo-2,3-dihydroindole-1-carbonyl chloride) and their pharmaceutically acceptable salts which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer (no data). In I, R1 and R2 are independently H, halo, alkyl, alkylthio, nitro, trihalomethyl, hydroxy, hydroxyalkyl, alkoxy, cyano, aryl, heteroaryl, -C(O)R7 (R7 is alkyl, amino, hydroxy, alkoxy, aryl, heteroaryl, aryloxy, heteroaryloxy, heterocycle, and aminoalkylamino), -NR8R9, -NR8C(O)R9, -SO2R8, and -S(O)2NR8R9 (R8 and R9 are independently H, alkyl, aryl and heteroaryl, or R8 and R9 together with the N to which they are attached form a saturated heterocycloamino). R3 is H, alkyl, hydroxyalkyl, aminoalkyl, -C(O)R7, aryl, and heteroaryl; R4 is H, alkyl, -C(O)R7 aryl, and heteroaryl. R5 is H and -COR10 where R10 is alkyl, alkoxy, hydroxy, aryl, aryloxy, heteroaryl, heterocycle, alkylamino, dialkylamino, or -NR11R12 where R11 is H or alkyl, and R12 is aminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, heteroaralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy group(s); or R4 and R5 together form - (CH2)4- or -(CH2)mCO(CH2)n- wherein n is 0 to 3, provided that n+m is 3. R6 is: (c) -OR13 wherein R13 is alkyl, trifluoromethyl, carboxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, hydroxyalkyl, alkoxyalkyl, aryl,

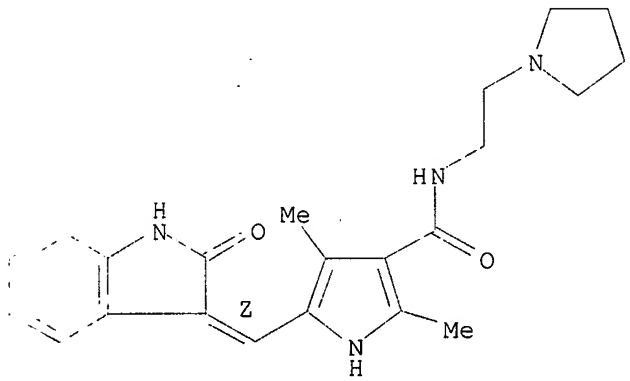
heteroaryl, heteroaralkyl, heterocyclyl, monosaccharides and heterocyclylalkyl wherein the alkyl chain in carboxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, heteroaralkyl, heterocyclylalkyl, hydroxyalkyl, or alkoxyalkyl is optionally substituted with one or two hydroxy group(s) and further wherein one or two C atoms in said alkyl chain are optionally replaced by O, -NR14- (R14 is H or alkyl), -S-, or -SO2-; or. (d) -NR15R16 where are R15 and R16 are independently H, alkyl, carboxyalkyl, alkoxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, hydroxyalkyl, aryl, heteroaryl, heteroaralkyl, and heterocyclylalkyl; wherein the alkyl chain in carboxyalkyl, aminoalkyl, phosphonooxyalkyl, heteroaralkyl, heterocyclylalkyl, hydroxyalkyl, or alkoxyalkyl is optionally substituted with one or two hydroxy group(s) and further wherein one or two C atoms in the alkyl chain are optionally replaced by O, -NR17- (R17 is H or alkyl), -S-, or -SO2-; or R15 and R16 together with the N atom to which they are attached form saturated or unsatd. heterocycloamino;. Although the methods of preparation are not claimed, >80 example prepns. are included, both of I and the unprotected version of I in which the C(O)R6 group has been replaced by H.

IT 356068-94-5P, 5-(5-Fluoro-2-oxo-1,2-dihydroindol-(3Z)-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-(pyrrolidin-1-yl)ethyl)amide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of prodrugs of (pyrrolylmethylidene)indolinones and activity as modulators of protein kinases)

RN 356068-94-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

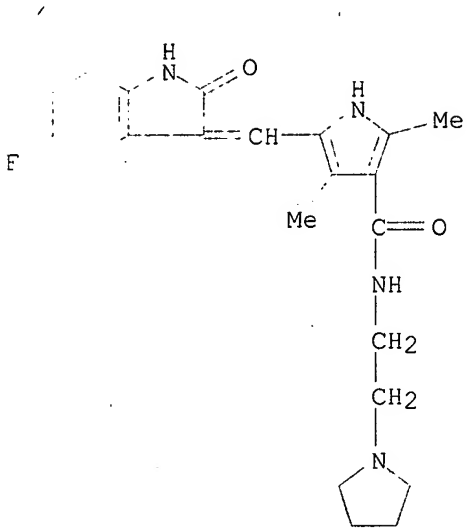
Double bond geometry as shown.



IT 346405-32-1P, 5-(5-Fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-(pyrrolidin-1-yl)ethyl)amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase modulator; preparation of prodrugs of (pyrrolylmethylidene)indolinones and activity as modulators of protein kinases)

RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:541364 HCAPLUS
DOCUMENT NUMBER: 138:147266
TITLE: Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors
AUTHOR(S): Liao, Albert T.; Chien, May B.; Shenoy, Narmada; Mendel, Dirk B.; McMahon, Gerald; Cherrington, Julie M.; London, Cheryl A.
CORPORATE SOURCE: Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California at Davis, Davis, CA, 95616, USA
SOURCE: Blood (2002), 100(2), 585-593
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mutations in the proto-oncogene c-kit, including point mutations, deletions, or duplications in the neg. regulatory juxtamembrane (JM) domain or point mutations in the catalytic domain, have been observed in human and canine cancers and often result in constitutive activation of Kit in the absence of ligand binding. To identify a receptor tyrosine kinase (RTK) inhibitor capable of blocking the function of mutant Kit, we evaluated 3 indolinones (SU11652, SU11654, and SU11655) that act as competitive inhibitors of ATP binding to several members of the split kinase family of RTKs, including VEGFR, FGFR, PDGFR, and Kit. Mast cell lines expressing either wildtype (WT) Kit, a point mutation in the JM domain, a tandem duplication in the JM domain, or a point mutation in the catalytic domain were used for these studies. All 3 indolinones inhibited phosphorylation of WT Kit in the presence of stem cell factor at concns. as low as 0.01 μM. Autophosphorylation of both JM mutants was inhibited at 0.01 to 0.1 μM, resulting in cell cycle arrest within 24 h, whereas autophosphorylation of the catalytic domain mutant was inhibited at 0.25 to 0.5 μM, resulting in cell death within 24 h. Poly(ADP-ribose) polymerase (PARP) cleavage was noted in all Kit mutant

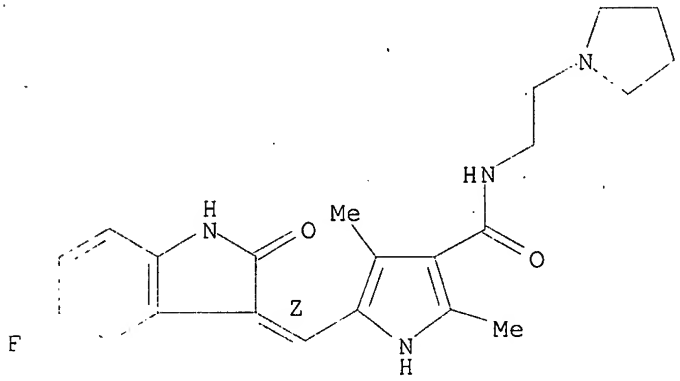
lines after indolinone treatment. In summary, SU11652, SU11654, and SU11655 are effective RTK inhibitors capable of disrupting the function of all forms of mutant Kit. Because the concns. of drug necessary for receptor inhibition are readily achievable and nontoxic in vivo, these compds. may be useful in the treatment of spontaneous cancers expressing Kit mutations.

IT 356068-94-5, SU 11654
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors)

RN 356068-94-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:617993 HCAPLUS
DOCUMENT NUMBER: 135:195497
TITLE: Preparation of pyrrole substituted 2-indolinone protein kinase inhibitors for treatment of cancer
INVENTOR(S): Tang, Peng Cho; Miller, Todd; Li, Xiaoyuan; Sun, Li; Wei, Chung Chen; Shirazian, Shahrzad; Liang, Congxin; Vojkovsky, Tomas; Nematalla, Asaad S.
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060814	A2	20010823	WO 2001-US4813	20010215
WO 2001060814	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2399358	AA	20010823	CA 2001-2399358		20010215
CA 2399358	C	20060321			
US 2002156292	A1	20021024	US 2001-783264		20010215
US 6573293	B2	20030603			
EP 1255752	A2	20021113	EP 2001-914376		20010215
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JP 2003523340	T2	20030805	JP 2001-560198		20010215
JP 3663382	B2	20050622			
BR 2001008394	A	20040622	BR 2001-8394		20010215
NZ 520640	A	20050429	NZ 2001-520640		20010215
AU 2001239770	B2	20060105	AU 2001-239770		20010215
NO 2002003831	A	20021015	NO 2002-3831		20020813
ZA 2002006469	A	20031113	ZA 2002-6469		20020813
BG 107078	A	20030430	BG 2002-107078		20020910
US 2004063773	A1	20040401	US 2003-412690		20030414
US 2005176802	A1	20050811	US 2005-28477		20050104
PRIORITY APPLN. INFO.:			US 2000-182710P	P	20000215
			US 2000-216422P	P	20000706
			US 2000-243532P	P	20001027
			US 2001-783264	A3	20010215
			WO 2001-AU4813	W	20010215
			WO 2001-US4813	W	20010215
			US 2003-412690	A1	20030414

OTHER SOURCE(S): MARPAT 135:195497

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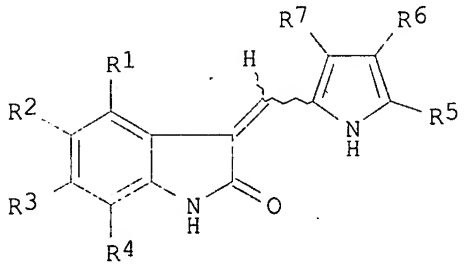

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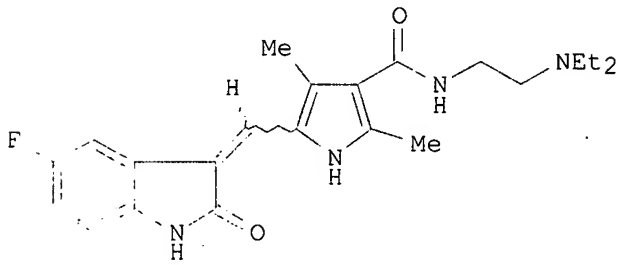


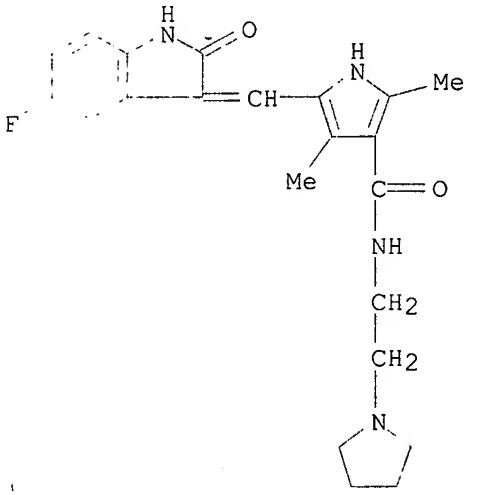
II

AB The title compds. (I) [wherein R1 = H, halo, (cyclo)alkyl, (hetero)aryl, heteroalicyclic, OH, alkoxy, acyl, (un)substituted amino or carbamoyl, etc.; R2 = H, halo, alkyl, trihalomethyl, OH, alkoxy, CN, (hetero)aryl, (un)substituted amino, acyl(amino), or sulfamoyl, etc.; R3 = H, halo, alkyl, trihalomethyl, OH, alkoxy, (hetero)aryl, (un)substituted acyl, (acyl)amino, sulfamoyl, or alkylsulfonyl, etc.; R4 = H, halo, alkyl, OH, alkoxy, or (un)substituted amino; R5 and R6 = independently H, alkyl, or acyl; R7 = H, alkyl, (hetero)aryl, or acyl; and their pharmaceutically acceptable salts] were prepared as protein kinase modulators for the treatment of cellular disorders such as cancer. For example, 5-fluoro-1,3-dihydroindol-2-one was condensed with 5-formyl-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide to give II (55%). II exhibited comparable activity against Flk-1 and PDGFRβ and inhibited PDGF-dependent receptor phosphorylation in cells with an IC50 value of approx. 0.03 μM. In efficacy expts. against various cancers in mice, II was well tolerated at 80 mg/kg/day, even when dosed continuously for more than 100 days.

IT 346405-32-1P 356068-94-5P 356069-21-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

RN 346405-32-1 HCAPLUS

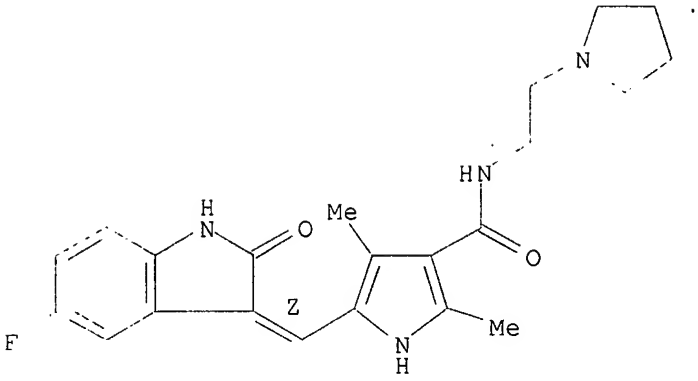
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 356068-94-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 356069-21-1 HCAPLUS
CN Butanedioic acid, hydroxy-, (2S)-, compd. with 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

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CRN 346405-32-1
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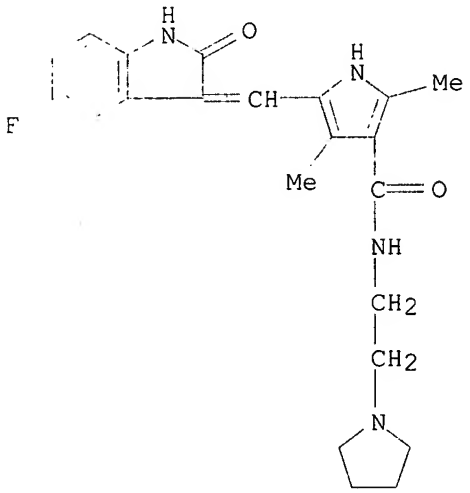
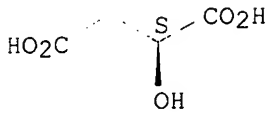


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:472477 HCAPLUS
DOCUMENT NUMBER: 135:56059
TITLE: Methods of modulating c-kit tyrosine protein kinase function with indolinone compounds
INVENTOR(S): Lipson, Ken; McMahon, Gerald
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045689	A2	20010628	WO 2000-US35009	20001222
WO 2001045689	A3	20020103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395461	AA	20010628	CA 2000-2395461	20001222
US 2002010203	A1	20020124	US 2000-741842	20001222
EP 1255536	A2	20021113	EP 2000-991704	20001222
EP 1255536	B1	20060628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500363	T2	20040108	JP 2001-546428	20001222
NZ 519697	A	20040827	NZ 2000-519697	20001222
AU 784266	B2	20060302	AU 2001-34363	20001222
AT 331514	E	20060715	AT 2000-991704	20001222
US 2004002534	A1	20040101	US 2003-600868	20030623
US 2005288353	A1	20051229	US 2005-205474	20050816

PRIORITY APPLN. INFO.:

US 1999-171693P	P	19991222
US 2000-741842	B1	20001222
WO 2000-US35009	W	20001222
US 2003-600868	A1	20030623

OTHER SOURCE(S): MARPAT 135:56059

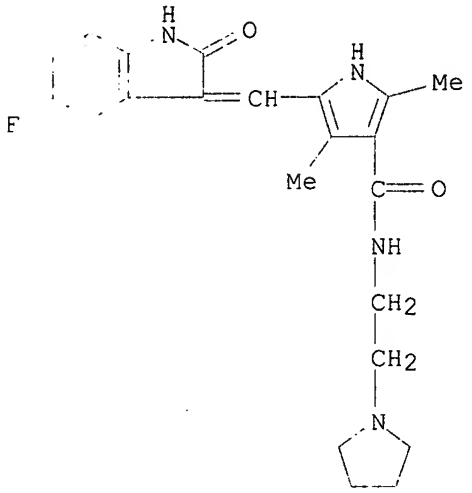
AB The invention concerns indolinone compds. and their use to inhibit the activity of a receptor tyrosine kinase. The invention is preferably used to treat cell proliferative disorders such as cancers characterized by over-activity or inappropriate activity of c-kit kinase.

IT 346405-32-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(indolinone derivs. for c-kit tyrosine protein kinase function modulation)

RN 346405-32-1 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



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=> s l3 and polymorph
            16 L3
          7488 POLYMORPH
          8573 POLYMORPHS
         13081 POLYMORPH
                (POLYMORPH OR POLYMORPHS)
L5           1 L3 AND POLYMORPH

=> d ibib

L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:740292  HCAPLUS
DOCUMENT NUMBER:          141:265970
TITLE:                    Polymorphs of pyrrole-substituted
                          2-indolinone protein kinase inhibitors
INVENTOR(S):              Sun, Changquan; Foster, Todd P.; Han, Fusen; Hawley,
                          Michael; Thamann, Tom
PATENT ASSIGNEE(S):       Pharmacia & Upjohn Company, USA
SOURCE:                   PCT Int. Appl., 36 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004076410         A2    20040910    WO 2004-US5281          20040223
     WO 2004076410         A3    20050303
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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     NO 2005004071        A     20051013    NO 2005-4071            20050901
PRIORITY APPLN. INFO.:                      US 2003-448863P     P   20030224
                                            US 2004-776337      A   20040212
                                            WO 2004-US5281      A   20040223


=> s l3 and crystal?
          16 L3
     1776048 CRYSTAL?
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     2076415 CRYSTAL?
                (CRYSTAL? OR CRYST OR CRYSTD OR CRYSTG OR CRYSTN)
L6         1 L3 AND CRYSTAL?

=> d ibib

L6   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:740292  HCAPLUS
DOCUMENT NUMBER:          141:265970
TITLE:                    Polymorphs of pyrrole-substituted 2-indolinone protein
                          kinase inhibitors
INVENTOR(S):              Sun, Changquan; Foster, Todd P.; Han, Fusen; Hawley,
                          Michael; Thamann, Tom
PATENT ASSIGNEE(S):       Pharmacia & Upjohn Company, USA
SOURCE:                   PCT Int. Appl., 36 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004076410         A2    20040910    WO 2004-US5281          20040223
     WO 2004076410         A3    20050303
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PRIORITY APPLN. INFO.:                       US 2003-448863P      P  20030224
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                                             WO 2004-US5281       A  20040223


=> s l3 and solid
           16 L3
      1033329 SOLID
       285687 SOLIDS
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                (SOLID OR SOLIDS)
L7          0 L3 AND SOLID

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   91.63     258.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -12.00     -12.00

STN INTERNATIONAL LOGOFF AT 09:02:29 ON 19 SEP 2006
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